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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,752	10/03/2003	Jonathan S. Stamler	2172	4905

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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/677,752	STAMLER, JONATHAN S.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 July 2006 and 22 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33 and 35-37 is/are pending in the application.
- 4a) Of the above claim(s) 35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33, 36 and 37 is/are rejected.
- 7) ☒ Claim(s) 33 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☒ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413) |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) ☒ Information Disclosure Statement(s) (PTO/SB/08) | 5) ☐ Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>22 February 2005</u> . | 6) ☐ Other: _____ |

DETAILED ACTION

Claims 33 and 35-37 are presented for examination.

Applicant's Amendment and remarks filed July 18, 2006 and response filed November 22, 2006 to the election of species requirement dated September 25, 2006 have each been received and entered into the present application.

Claims 33 and 35-37 are pending. Claims 1-32, 34 and 38-44 are cancelled and claim 33 is amended.

Applicant's arguments and amendments to the claims, filed July 18, 2006, have been fully considered. In view of the claim amendments, the previous rejections have been withdrawn. The following rejections and objections are newly applied to the amended claim set. They constitute the complete set of rejections and objections presently being applied to the instant application.

Requirement for Restriction/Election

Applicant's election with traverse of the species of amyotrophic lateral sclerosis as the neurodegenerative disease associated with a receptor having a cysteine residue or other cysteine containing protein that is modified by a thiol reactive agent to inhibit its function, and the species of NO donors as the thiol reactive agent, wherein S-nitrosoglutathione was elected as a specific species of NO donor, in the reply filed November 22, 2006, is acknowledged by the Examiner.

Applicant traverses the requirement on the grounds that if members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire group in the claim can be made without serious burden, then the Examiner must examine all members of the group.

Applicant's traversal has been carefully considered in its entirety, but fails to be persuasive.

In particular, it is noted that though Applicant is asserting that the present search may be made without serious burden to the Examiner, Applicant has not presented any evidence or argument to this

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effect. Accordingly, in the absence of any evidence to the contrary, it remains that a search for the entire breadth and scope of the present claims precludes a quality examination on the merits due to the burdensome search that would be required, for the reasons previously made of record (see, e.g., pages 2-7 of the requirement dated September 25, 2006). Further, it is noted that the disparate nature of, for example, the thiol reactive agents, would necessarily encompass a burdensome search due to their highly variable chemical, functional and structural nature and also that the art does not recognize such compounds as being chemical, structural or functional equivalents of one another. Accordingly, the requirement for election remains proper and is maintained.

Therefore, for the reasons above and those made of record at pages 2-7 of the previous Office Action dated September 25, 2006, the election requirement is deemed proper and is made **FINAL**.

Claim 35 is **withdrawn** from further consideration pursuant to 37 C.F.R. 1.142(b), as being drawn to a non-elected invention.

The claims corresponding to the elected subject matter are claims 33 and 36-37 and such claims are herein acted on the merits.

Information Disclosure Statement of February 11, 2005

Applicant has requested clarification in the remarks filed July 18, 2006 as to why the Nozik-Grayck et al. reference denoted as "C1" on the Information Disclosure Statement (IDS) filed February 11, 2005 was not considered by the Examiner.

In response thereto, and following a review of the contents of the instant application, it is apparent that the Examiner's failure to consider this document was in error. Please see the attached, completed copy of the IDS of February 11, 2005, which acknowledges consideration of the reference.

Objections to the Claims (New Grounds of Objection)

Claim 33 is objected to for failing to define the acronym "NO" at its first occurrence in the claims.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33 and 36-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 33 is directed to a method for the treatment of a patient with a neurodegenerative disease associated with a receptor having a cysteine residue or other cysteine containing protein that is modified by a thiol reactive agent to inhibit its function, or at risk therefor, wherein said neurodegenerative disease is amyotrophic lateral sclerosis, comprising the administration to said patient a therapeutically effective amount of said thiol reactive agent, wherein said thiol reactive agent is S-nitrosoglutathione and is administered in an amount that provides a submicromolar concentration of NO or NO donor in the patient's blood.

In particular, the recitation of the administration of a therapeutically effective amount of a thiol reactive agent as stated in, for example, claim 33, fails to delineate the function of the therapeutically effective amount. It is necessarily implied from the present claims as written that the amount to be administered is intended for use to elicit a therapeutic effect. However, it is not clear as to what condition(s), disease(s) or disorder(s) of the host upon which said amount is capable of exerting a therapeutic effect. Applicant's failure to define for what the amount is therapeutically effective renders the claim vague and indefinite.

Additionally, it is noted that present claim 33 also recites the limitation “or at risk therefor”, but it is unclear as to whether such a limitation is intended to limit the patient with the neurodegenerative disease. Furthermore, since the patient of the claims is required to have or be suffering from a neurodegenerative disease associated with a receptor having a cysteine residue or other cysteine containing protein that is modified by a thiol reactive agent to inhibit its function, it is unclear how the patient could also be “at risk therefor”. Accordingly, it is unclear exactly how Applicant intends for the limitation “or at risk therefor” to limit the presently claimed invention.

For these reasons, the metes and bounds of the present claims cannot be identified and one of ordinary skill in the art would not necessarily be reasonably apprised of the scope of the claims. In light of such, claims 33 and 36-37 fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 33 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipton (WO 94/06428; 1994).

Lipton teaches a method for decreasing NMDA receptor complex-mediated neuronal damage in a mammal by administering to the mammal a nitroso-compound that generates nitric oxide, or a related redox species such as NO⁻ or NO⁺ equivalent, in a concentration effective to effect neuroprotection in a mammal (abstract) who is suffering from a neurodegenerative disease (page 4, lines 4-9), such as, e.g., amyotrophic lateral sclerosis (i.e., “ALS”; page 4, line 7), and the nitroso-compound (page 6, line 1-page

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7, line 2) is, e.g., S-nitrosoglutathione (page 6, line 12), and discloses exemplary therapeutic dosages (page 27, lines 21-27). Lipton further teaches that the disclosed neurodegenerative diseases may also result from stimulation of the NMDA-receptor channel complex by other excitatory amino acids, such as cysteine (page 11, lines 13-21). Please also see claims 1, 5, 6 and 9 of Lipton at pages 39-41.

Though Lipton does not expressly teach that neurodegenerative disease (i.e., amyotrophic lateral sclerosis) is associated with a cysteine protease in a nerve cell and that the administration of S-nitrosoglutathione would solely affect an allosteric cysteine (claims 36-37), the administration of the same nitro-compound as claimed (i.e., S-nitrosoglutathione) to the same host as that claimed (i.e., a patient suffering from amyotrophic lateral sclerosis) is considered to necessarily have the claimed effect on an allosteric cysteine, whether recognized by Lipton or not. Products of identical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

Further, the very fact that Lipton teaches the identical neurodegenerative disease (i.e., amyotrophic lateral sclerosis) as that claimed and also teaches a possible association with the excitatory amino acid cysteine (see page 11, lines 13-21), the presently claimed association with a receptor having a cysteine residue that is modified by a thiol reactive agent is also necessarily present, since the same disease cannot have distinct mechanistic or pathophysiologic properties.

Lastly, Lipton teaches therapeutically effective amounts to treat the neurodegenerative disease (i.e., amyotrophic lateral sclerosis) and, therefore, meets the limitations of present claim 33. Although Lipton does not expressly acknowledge the fact that the amount is sufficient to provide a submicromolar concentration of nitric oxide in the blood of the patient, such is a functional end result of administering the compound. Accordingly, the administration of the identical compound S-nitrosoglutathione to the same ALS patient in a therapeutically effective amount would also result in a submicromolar nitric oxide blood concentration, absent factual evidence to the contrary.

Double Patenting (New Grounds of Rejection)

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33 and 36-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5-6 and 9 of copending U.S. Patent Application No. 11/545,049.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the copending claims and those of the present application are not considered to be patentably distinct from each other because the present claims clearly anticipate the copending claims. The present claims clearly provide for the treatment of a patient suffering from the neurodegenerative disease amyotrophic lateral sclerosis by administering to said patient an effective amount of the compound S-nitrosoglutathione. Though the copending additionally recite that the neurodegenerative disease is associated with a need for decreasing NMDA receptor-

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mediated neuronal damage, where the present claims are silent as to such a need or effect, it remains that the present claims clearly recognize a beneficial therapeutic effect on amyotrophic lateral sclerosis using the compound S-nitrosoglutathione, and, therefore, whatever mechanism by which such a compound exerts such ameliorating effects on the disease are considered to be necessarily present because the administration of the same compound as claimed to the same host as claimed must necessarily have the same NMDA receptor-mediated neuronal damage reducing properties, whether recognized at the time of filing of the present application or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

Accordingly, rejection of present claims 33 and 36-37 is proper over claims 1, 5-6 and 9 of copending U.S. Patent Application No. 11/545,049 as claiming obvious and unpatentable variants thereof.

Conclusion

Rejection of claims 33 and 36-37 is proper and is **maintained**.

Claim 35 remains **withdrawn** from consideration pursuant to 37 C.F.R. 1.142(b).

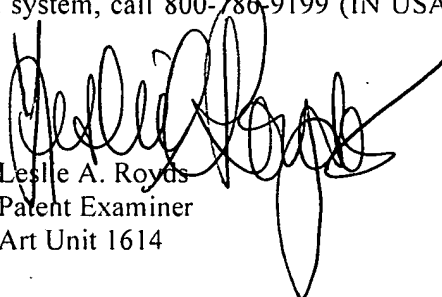
No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

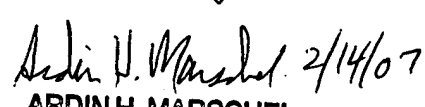
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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Leslie A. Royds
Patent Examiner
Art Unit 1614

February 7, 2007



ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER